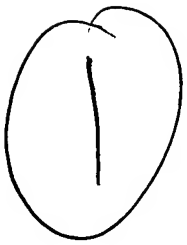


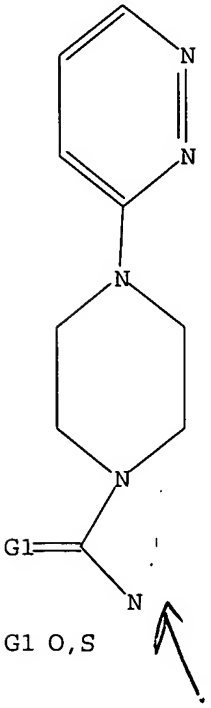
1-13 4-7 13-14 13-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 1-13 2-3 3-4 4-5 4-7 5-6 13-14 13-17
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

G1:O,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 15:26:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS 2 ANSWERS

<09/21/2005> Habte

```
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            4 TO      200
PROJECTED ANSWERS:               2 TO      124

L2            2 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 15:27:09 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      127 TO ITERATE

100.0% PROCESSED      127 ITERATIONS                              58 ANSWERS
SEARCH TIME: 00.00.01

L3            58 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                161.33     161.54

FILE 'CAPLUS' ENTERED AT 15:27:15 ON 21 SEP 2005
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FILE LAST UPDATED: 20 Sep 2005  (20050920/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l3
L4            6 L3

=> d ibib abs hitstr tot
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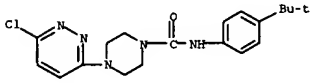
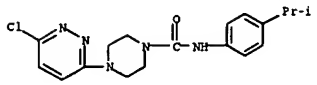
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:863095 CAPLUS
DOCUMENT NUMBER: 142:56256
TITLE: Synthesis and evaluation of pyridazinylpiperazines as vanilloid receptor 1 antagonists
AUTHOR(S): Tafesse, Laykea; Sun, Qun; Schmid, Lori; Valenzano, Kenneth J.; Rotshteyn, Yakov; Su, Xin; Kyle, Donald J.
CORPORATE SOURCE: Discovery Research, Purdue Pharma L.P., Cranbury, NJ, 08512, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(22), 5513-5519
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:56256
AB A structurally biased chemical library of pyridazinylpiperazine analogs was prepared in an effort to improve the pharmaceutical and pharmacol. profile of the lead compound N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)tetrahydropyrazine-1(2H)-carboxamide (BCTC). The library was evaluated for VR1 antagonist activity in capsaicin-induced and pH 5.5-induced FLIPR assays in a human VR1-expressing HEK293 cell line. The most potent VR1 antagonists have IC50 values of 9-200 nM with improved pharmaceutical and pharmacol. profiles vs. the lead BCTC. These compds. represent possible second-generation BCTC analogs.
IT **808196-38-5P 808196-39-6P 808196-40-9P**
808196-41-0P 808196-42-1P 808196-53-4P
808196-55-6P 808196-57-8P 808196-58-9P
808196-59-0P 808196-61-4P 808196-62-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and evaluation of pyridazinylpiperazines as vanilloid receptor 1 antagonists)
RN 808196-38-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-3-pyridazinyl)-N-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-39-6 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-3-pyridazinyl)-N-[4-(1-methylethyl)phenyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 808196-40-9 CAPLUS
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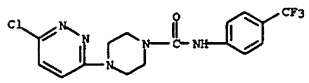
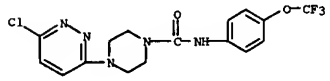
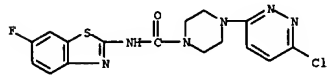


RN 808196-41-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)

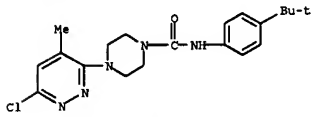


RN 808196-42-1 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-3-pyridazinyl)-N-(6-fluoro-2-benzothiazolyl)- (9CI) (CA INDEX NAME)

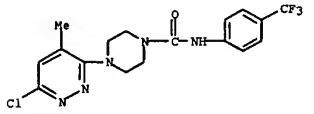


RN 808196-53-4 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)

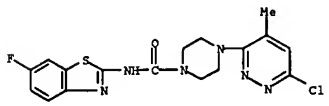
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



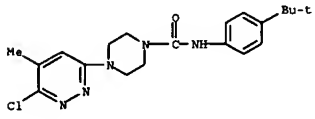
RN 808196-55-6 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-57-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-(6-fluoro-2-benzothiazolyl)- (9CI) (CA INDEX NAME)

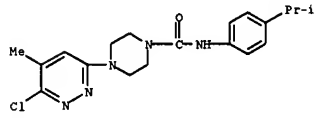


RN 808196-58-9 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)

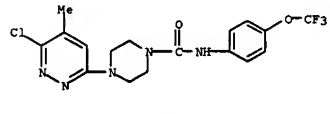


RN 808196-59-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-[4-(1-methylethyl)phenyl]- (9CI) (CA INDEX NAME)

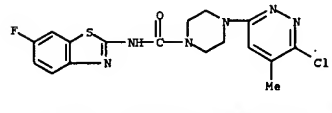
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 808196-61-4 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-62-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-(6-fluoro-2-benzothiazolyl)- (9CI) (CA INDEX NAME)



IT **652990-54-0P 652990-55-1P 652990-56-2P**
652990-57-3P 652990-58-4P 652990-59-5P
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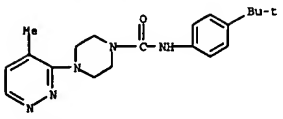
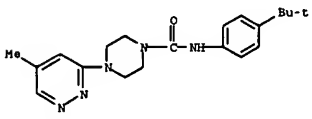
808196-52-3P 808196-64-7P 808196-65-8P
808196-66-9P 808196-67-0P 808196-73-8P
808196-74-9P 808196-75-0P 808196-76-1P
808196-77-2P 808196-78-3P 808196-79-4P
808196-80-7P 808196-81-8P 808196-87-4P
808196-88-5P 808196-89-6P 808196-90-9P
808196-91-0P 808196-92-1P 808196-93-2P
808196-94-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of pyridazinylpiperazines as vanilloid receptor 1 antagonists)
RN 652990-54-0 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

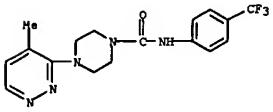
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



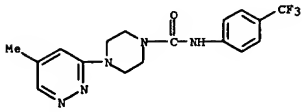
RN 652990-55-1 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(5-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



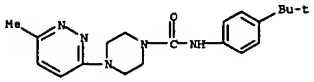
RN 652990-56-2 CAPLUS
CN 1-Piperazinecarboxamide, 4-(4-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



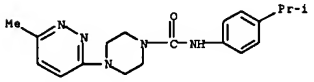
RN 652990-57-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-(5-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



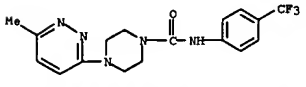
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



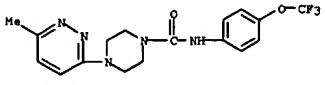
RN 808196-44-3 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1-methylethyl)phenyl]-4-(6-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



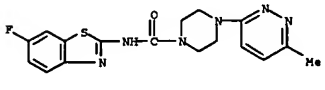
RN 808196-45-4 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-46-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



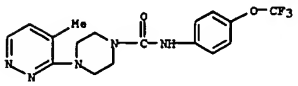
RN 808196-47-6 CAPLUS
CN 1-Piperazinecarboxamide, N-(6-fluoro-2-benzothiazolyl)-4-(6-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



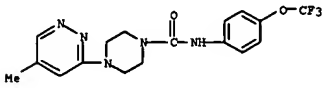
RN 808196-52-3 CAPLUS

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 652990-58-4 CAPLUS
CN 1-Piperazinecarboxamide, 4-(4-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)

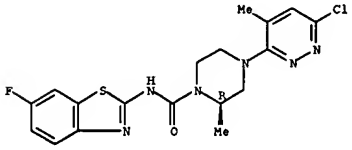


RN 652990-59-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(5-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 722498-19-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-(6-fluoro-2-benzothiazolyl)-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

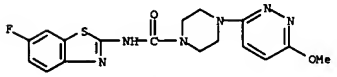
Absolute stereochemistry.



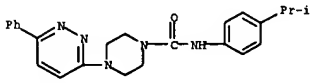
RN 808196-43-2 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(6-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

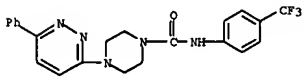
CN 1-Piperazinecarboxamide, N-(6-fluoro-2-benzothiazolyl)-4-(6-methoxy-3-pyridazinyl)- (9CI) (CA INDEX NAME)



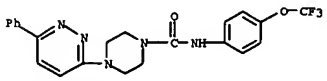
RN 808196-64-7 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1-methylethyl)phenyl]-4-(6-phenyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



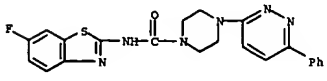
RN 808196-65-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-phenyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-66-9 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-phenyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)

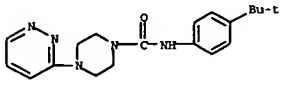


RN 808196-67-0 CAPLUS
CN 1-Piperazinecarboxamide, N-(6-fluoro-2-benzothiazolyl)-4-(6-phenyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

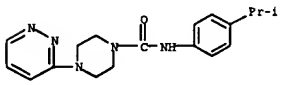


L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

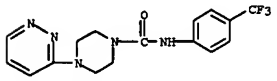
RN 808196-73-8 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(3-pyridazinyl)-(9CI) (CA INDEX NAME)



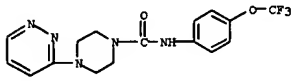
RN 808196-74-9 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1-methylethyl)phenyl]-4-(3-pyridazinyl)-(9CI) (CA INDEX NAME)



RN 808196-75-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-(3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)

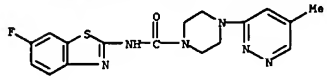


RN 808196-76-1 CAPLUS
CN 1-Piperazinecarboxamide, 4-(3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]-(9CI) (CA INDEX NAME)

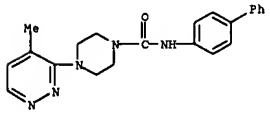


RN 808196-77-2 CAPLUS
CN 1-Piperazinecarboxamide, N-(6-fluoro-2-benzothiazolyl)-4-(3-pyridazinyl)-(9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

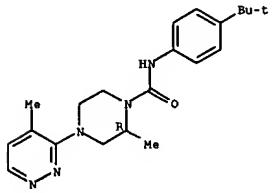


RN 808196-87-4 CAPLUS
CN 1-Piperazinecarboxamide, N-[1,1'-biphenyl]-4-yl-4-(4-methyl-3-pyridazinyl)-(9CI) (CA INDEX NAME)



RN 808196-88-5 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-methyl-4-(4-methyl-3-pyridazinyl)-, (2R)- (9CI) (CA INDEX NAME)

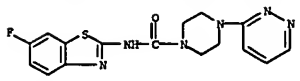
Absolute stereochemistry.



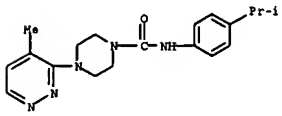
RN 808196-89-6 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-methyl-4-(5-methyl-3-pyridazinyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

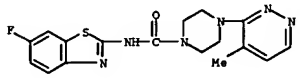
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



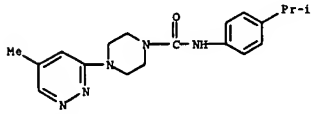
RN 808196-78-3 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1-methylethyl)phenyl]-4-(4-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



RN 808196-79-4 CAPLUS
CN 1-Piperazinecarboxamide, N-(6-fluoro-2-benzothiazolyl)-4-(4-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

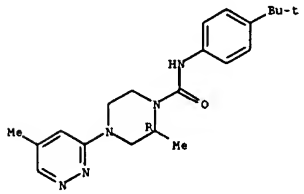


RN 808196-80-7 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1-methylethyl)phenyl]-4-(5-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



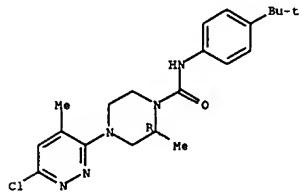
RN 808196-81-8 CAPLUS
CN 1-Piperazinecarboxamide, N-(6-fluoro-2-benzothiazolyl)-4-(5-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 808196-90-9 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-[4-(1,1-dimethylethyl)phenyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

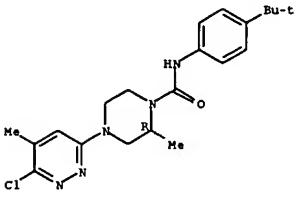
Absolute stereochemistry.



RN 808196-91-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-[4-(1,1-dimethylethyl)phenyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

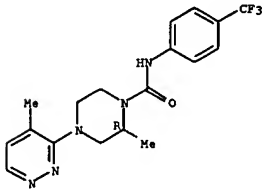
Absolute stereochemistry.

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 808196-92-1 CAPLUS
CN 1-Piperazinecarboxamide, 2-methyl-4-(4-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]-, (2R)- (9CI) (CA INDEX NAME)

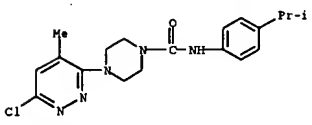
Absolute stereochemistry.



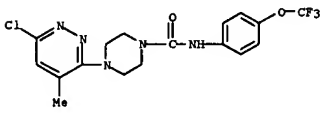
RN 808196-93-2 CAPLUS
CN 1-Piperazinecarboxamide, 2-methyl-4-(5-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

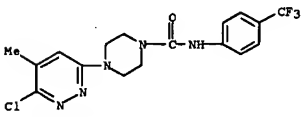
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



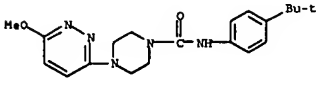
RN 808196-56-7 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



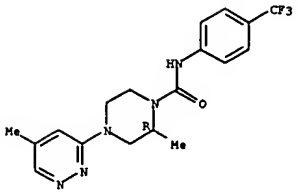
RN 808196-60-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT 808196-48-7P 808196-49-8P 808196-50-1P
808196-51-2P 808196-63-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and evaluation of pyridazinylpiperazines as vanilloid receptor 1 antagonists)
RN 808196-48-7 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(6-methoxy-3-pyridazinyl)- (9CI) (CA INDEX NAME)

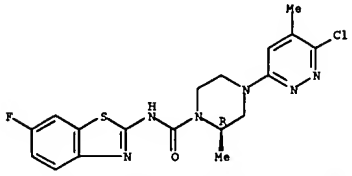


L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



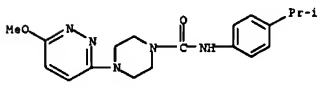
RN 808196-94-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-5-methyl-3-pyridazinyl)-N-(6-fluoro-2-benzothiazolyl)-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

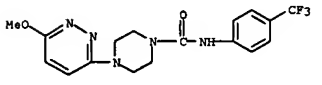


IT 808196-54-5P 808196-56-7P 808196-60-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and evaluation of pyridazinylpiperazines as vanilloid receptor 1 antagonists)
RN 808196-54-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-[4-(1-methylethyl)phenyl]- (9CI) (CA INDEX NAME)

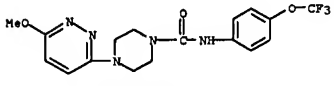
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 808196-49-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-methoxy-3-pyridazinyl)-N-[4-(1-methylethyl)phenyl]- (9CI) (CA INDEX NAME)



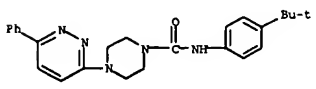
RN 808196-50-1 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-methoxy-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-51-2 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-methoxy-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 808196-63-6 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(6-phenyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

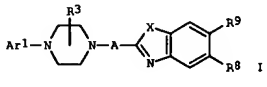


REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:566601 CAPLUS
DOCUMENT NUMBER: 141:123640
TITLE: Heterocyclylpiperazinylbenzothiazoles, heterocyclylpiperazinylbenzimidazoles, and heterocyclylpiperazinylbenzooxazoles prepared as antagonists for the metabotropic glutamate receptors mGluR1 and mGluR5 and as ligands for human VR1
INVENTOR(S): Sun, Qun; Tafesse, Laykea; Victory, Sam
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 705 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058754	A1	20040715	WO 2003-US41100	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004186111	A1	20040923	US 2003-739190	20031219
PRIORITY APPLN. INFO.:			US 2002-435917P	P 20021224
			US 2003-459626P	P 20030403
			US 2003-473856P	P 20030529

OTHER SOURCE(S): MARPAT 141:123640
GI



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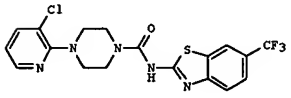
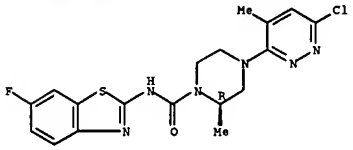


II

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Heterocyclylpiperazinyl benzothiazoles, benzimidazoles, and benzooxazoles I [A = bond, C(:O)NR4, C(:S)NR4; Ar1 = (un)substituted pyridinyl, pyrazinyl, thiadiazolyl, pyrimidinyl, or pyridazinyl; R3 = H, Me, halogen, cyano, hydroxy, alkoxy, nitro, amino, etc.; X = S, O, NR10; R8, R9 = H, alkyl, alkenyl, alkynyl, cycloalkyl, Ph, halo, halomethyl, dihalomethyl, trihalomethyl, cyano, etc.; R10 = H, alkyl] such as II are prepared as antagonists for the metabotropic glutamate receptors mGluR1 and mGluR5 and as ligands for the protein VR1 for the treatment of pain, addiction, urinary incontinence, irritable-bowel disorder, inflammatory bowel disease, ulcers, Parkinson's disease, epilepsy, seizures, anxiety, psychosis, stroke, pruritus, cognitive disorders, memory deficits or restricted brain function, Huntington's chorea, amyotrophic lateral sclerosis, retinopathy, muscle spasms, migraines, vomiting, dyskinesia, and depression. Regioselective coupling of 2,3-dichloropyridine and piperazine yields 1-(3-chloro-2-pyridinyl)piperazine (III), while acylation of 6-(trifluoromethyl)-2-aminobenzothiazole with p-nitrophenyl chlorocarbonate yields p-nitrophenyl [6-(trifluoromethyl)-2-benzothiazolyl]carbamate (IV); coupling of III and IV yields II. II gives IC50 values of 262 and 51 (units not indicated) in pH-based and capsaicin-based assays (resp.) for binding to human VR1.
IT 722498-19-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
RN 722498-19-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-4-methyl-3-pyridazinyl)-N-(6-fluoro-2-benzothiazolyl)-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

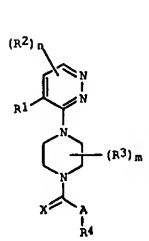


own work

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:101144 CAPLUS
DOCUMENT NUMBER: 140:146169
TITLE: Preparation of pyridazinylpiperazines as VR1 inhibitors for treating pain
INVENTOR(S): Kyle, Donald J.; Sun, Qun
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011441	A1	20040205	WO 2003-US23377	20030725
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235853	A1	20041125	US 2003-625708	20030724
PRIORITY APPLN. INFO.:			US 2002-398594P	P 20020726
			US 2002-411020P	P 20020917
			US 2002-413155P	P 20020925
			US 2002-416525P	P 20021008

OTHER SOURCE(S): MARPAT 140:146169
GI



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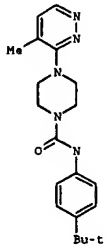
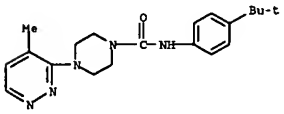


II

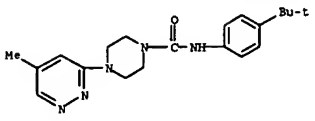
AB Title compds. I [wherein X = S or O; A = NH, N(alkyl), or N(alkoxy); R1 =

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
halo, Me, ON2, CN, OH, OMe, NH2, or halomethyl; R2 and R3 = independently halo, OH, NH2, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or (un)substituted heterocyclyl, Ph, naphthyl, or (hetero)aryl; or R3 = NO2; R4 = (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or (un)substituted heterocyclyl, Ph, naphthyl, or (hetero)aryl; m = 0-2; n = 0-2; and pharmaceutically acceptable salt thereof] were prepd. as vanilloid receptor 1 (VR1) inhibitors. For example, 3,6-dichloro-4-methylpyridazine was coupled with piperazine in DMSO to afford a mixt. of regioisomers, which was reacted with 4-tert-butylphenylisocyanate in DCM and hydrogenated with H2 over Pd in MeOH to provide II and its 5-Me isomer. In pH-based and capsaicin-based binding assays, II inhibited activity of the human VR1 receptor with IC50 values of 220.7 ± 50.4 nM and 47.2 ± 9.9 nM, resp. Thus, I and their pharmaceutical compns. are useful for treating or preventing pain, urinary incontinence (UI), inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), or an ulcer (no data).
IT 652990-54-0P, 4-(4-Methylpyridazin-3-yl)piperazine-1-carboxylic acid N-(4-tert-butylphenyl)amide 652990-55-1P, 4-(5-Methylpyridazin-3-yl)piperazine-1-carboxylic acid N-(4-tert-butylphenyl)amide 652990-56-2P, 4-(4-Methylpyridazin-3-yl)piperazine-1-carboxylic acid N-(4-trifluoromethylphenyl)amide 652990-57-3P, 4-(5-Methylpyridazin-3-yl)piperazine-1-carboxylic acid N-(4-trifluoromethylphenyl)amide 652990-58-4P, 4-(4-Methylpyridazin-3-yl)piperazine-1-carboxylic acid N-(4-trifluoromethoxyphenyl)amide 652990-59-5P, 4-(5-Methylpyridazin-3-yl)piperazine-1-carboxylic acid N-(4-trifluoromethoxyphenyl)amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(VR1 inhibitor; preparation of pyridazinylpiperazines as VR1 inhibitors for
treating pain and intestinal disorders)
RN 652990-54-0 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

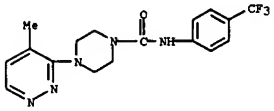


RN 652990-55-1 CAPLUS
CN 1-Piperazinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-4-(5-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)

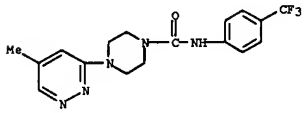
L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



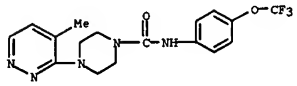
RN 652990-56-2 CAPLUS
CN 1-Piperazinecarboxamide, 4-(4-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 652990-57-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-(5-methyl-3-pyridazinyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

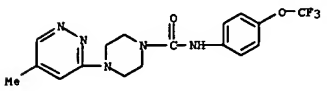


RN 652990-58-4 CAPLUS
CN 1-Piperazinecarboxamide, 4-(4-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 652990-59-5 CAPLUS

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 1-Piperazinecarboxamide, 4-(5-methyl-3-pyridazinyl)-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

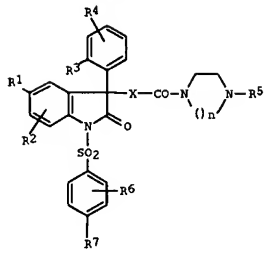
ACCESSION NUMBER: 2003:76773 CAPLUS
DOCUMENT NUMBER: 138:137337
TITLE: Preparation of N-phenylsulfonyl-1,3-dihydro-2H-indol-2-one derivatives containing piperazinylcarbonyl or homopiperazinylcarbonyl as vasopressin receptor inhibitors, their preparation and their therapeutic use
INVENTOR(S): Di Malta, Alain; Garcia, Georges; Roux, Richard; Schoentjes, Bruno; Serradeil-le Gal, Claudine; Tonnerre, Bernard; Wagnon, Jean
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008407	A2	20030130	WO 2002-FR2500	20020715
WO 2003008407	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2827604	A1	20030124	FR 2001-10359	20010717
FR 2827604	B1	20030919		
CA 2450437	AA	20030130	CA 2002-2450437	20020715
EP 1419150	A2	20040519	EP 2002-774822	20020715
EP 1419150	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011284	A	20040803	BR 2002-11284	20020715
CN 1533387	A	20040929	CN 2002-814262	20020715
JP 2004536131	T2	20041202	JP 2003-513966	20020715
NZ 530144	A	20050324	NZ 2002-530144	20020715
AT 294171	E	20050515	AT 2002-774822	20020715
ZA 2003009717	A	20041215	ZA 2003-9717	20031215
US 2004180878	A1	20040916	US 2004-484370	20040116
HK 1061679	A1	20050722	HK 2004-104546	20040625

PRIORITY APPLN. INFO.: FR 2001-10359 A 20010717
WO 2002-FR2500 W 20020715

OTHER SOURCE(S): MARPAT 138:137337
GI

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



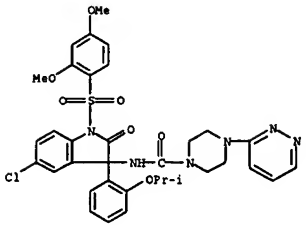
I

AB The invention concerns N-phenylsulfonyl-1,3-dihydro-2H-indole-2-one derivs. containing piperazinylcarbonyl or homopiperazinylcarbonyl (shown as I; variables defined below; e.g. 5-chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-3-(2-methoxyphenyl)-3-[2-oxo-2-[4-(4-pyridinyl)-1-piperazinyl]ethyl]-1,3-dihydro-2H-indol-2-one), as well as their addition salts with acids or organic salts, their solvates and/or hydrate(s), exhibiting affinity and selectivity for arginine-vasopressin V1b receptors and/or for oxytocin receptors, and further, for certain compds., an affinity for V1a receptors. The invention also concerns the method for preparing them, intermediate compds. (I without phenylsulfonyl) for their preparation, pharmaceutical compns. containing them and their use for preparing medicines. For I: n = 1 or 2; X = -CH2-, -O-, -NH-, -O-CH2-, -NH-CH2-, -NH-CH2-CH2-; R1 = halo, (C1-C4)alkyl, (C1-C4)alkoxy; R2 = H, halo, (C1-C4)alkyl, (C1-C4)alkoxy, trifluoromethyl; R3 = halo, (C1-C3)alkyl, (C1-C3)alkoxy, trifluoromethyl, trifluoromethoxy; R4 = H, halo, (C1-C3)alkyl, (C1-C3)alkoxy; R5 = pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazol-2-yl, oxazol-2-yl, imidazol-2-yl; R6 = (C1-C4)alkoxy; R7 = (C1-C4)alkoxy. Compds. I exhibit inhibition concns. (IC50) for V1a and V1b vasopressin receptors and for oxytocin receptors from 10-6 to 10-9 M and for V2 receptors better than 10-6 M. About 40 examples of intermediate prepns. and 92 examples of preparation of I are included.

IT 492431-50-2P, N-[5-Chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-3-(2-isopropoxyphenyl)-2-oxo-2,3-dihydro-1H-indol-3-yl]-4-(3-pyridazinyl)piperazine-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-phenylsulfonyldihydroindolone derivs. containing piperazinylcarbonyl or homopiperazinylcarbonyl as vasopressin receptor inhibitors, their preparation and their therapeutic use)

RN 492431-50-2 CAPLUS
CN 1-Piperazinecarboxamide, N-[5-chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-2,3-dihydro-3-[2-(1-methylethoxy)phenyl]-2-oxo-1H-indol-3-yl]-4-(3-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



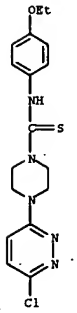
L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1972:400176 CAPLUS
DOCUMENT NUMBER: 77:176
TITLE: Thiourea derivatives with tuberculostatic action. II. Acylthiocarbamides
AUTHOR(S): Toldy, L.; Solyom, S.; Kocka, I.; Toth, G.; Toth, I.
CORPORATE SOURCE: Inst. Drug Res., Budapest, Hung.
SOURCE: Acta Chimica Academiae Scientiarum Hungaricae (1971), 69(2), 221-7
CODEN: ACASA2; ISSN: 0001-5407
DOCUMENT TYPE: Journal
LANGUAGE: German

AB Of the 21 1-(4-alkoxyphenylthiocarbamyl)-(4R)-piperazines, 15 1-substituted 3-acetylthiocarbamides, and 19 1-substituted S-methoxymethylisothiocarbamides tested for tuberculostatic activity, 1-(4-isoamyloxyphenyl)-3-carbethoxythiocarbamide (I) [23822-65-3] had the greatest effect in vitro, being tuberculostatic at 0.4-0.8 μg/ml, and it gave an expressed antituberculotic effect in mice and guinea pigs with no toxic effects. The absorptive properties of I were also good.

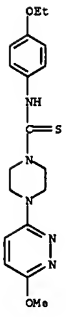
IT 36993-55-2 38313-50-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tuberculostatic activity of)

RN 36993-55-2 CAPLUS
CN 1-Piperazinecarbothioamide, 4-(6-chloro-3-pyridazinyl)-N-(4-ethoxyphenyl)- (9CI) (CA INDEX NAME)



RN 38313-50-7 CAPLUS
CN 1-Piperazinecarbothioamide, N-(4-ethoxyphenyl)-4-(6-methoxy-3-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

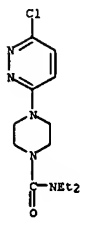
ACCESSION NUMBER: 1972:3796 CAPLUS
DOCUMENT NUMBER: 76:3796
TITLE: Piperazine derivatives. III. Diethylcarbamyl and xanthene derivatives
AUTHOR(S): Toldy, Lajos; Toth, Istvan; Borsy, Jozsef; Andrasi, Ferenc
CORPORATE SOURCE: Inst. Med. Res., Budapest, Hung.
SOURCE: Acta Chimica Academiae Scientiarum Hungaricae (1971), 70(1-2), 101-22
CODEN: ACASA2; ISSN: 0001-5407
DOCUMENT TYPE: Journal
LANGUAGE: German

GI For diagram(s), see printed CA Issue.

AB Substituted piperazines were prepared as anticholinergic agents for treating ulcers. Of 66 compds. prepared the 1-(9-xanthenecarbonyl)-4-[β-(4-alkyl-1-piperazinyl)ethyl]piperazines (I) [especially I (R = iso-Bu)] showed the best peroral resorption. In an example, 12.4 g 1-diethylcarbamoyl-4-(β-chloroethyl)piperazine was stirred for 3 hr at 130° with 22.12 g N-diethylcarbamoylpiperazine. The mixture was cooled, worked up, dissolved in MeOH and treated with alc. HCl to give 9.8 g II. Nineteen I (R = alkyl, CO2Et, Et2NCO, substituted aryl, CO2CH2Ph) were prepared analogously.

IT 34581-03-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 34581-03-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-(6-chloro-3-pyridazinyl)-N,N-diethyl- (9CI) (CA INDEX NAME)



2

1-13 4-7 13-14 13-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 1-13 2-3 3-4 4-5 4-7 5-6 13-14
exact bonds :
13-17
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

G1:O,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 17:CLASS

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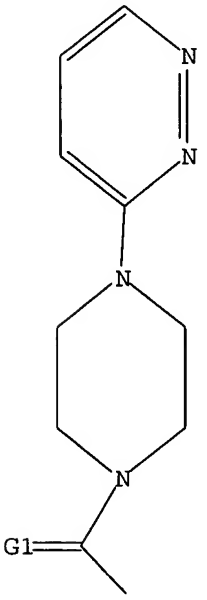

G1 O,S

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 44 TO ITERATE

<09/21/2005> Habte

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100.0% PROCESSED       44 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          483 TO     1277
PROJECTED ANSWERS:               3 TO      163

L2            3 SEA SSS SAM L1

=> s l1 sss full
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FULL SCREEN SEARCH COMPLETED -      614 TO ITERATE

100.0% PROCESSED      614 ITERATIONS                               26 ANSWERS
SEARCH TIME: 00.00.01

L3           26 SEA SSS FUL L1

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               161.33     161.54

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L4           12 L3

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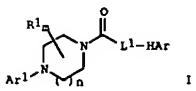
L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:540490 CAPLUS
DOCUMENT NUMBER: 143:78197
TITLE: Preparation of substituted piperazine derivatives as CCR1 receptor antagonists
INVENTOR(S): Pennell, Andrew M. K.; Aggen, James B.; Wright, J. J. Kim; Sen, Subhabrata; Mcmaster, Brian E.; Dairaghi, Daniel Joseph; Chen, Wei; Zhang, Penglie
PATENT ASSIGNEE(S): Chemocentryx, Inc., USA
SOURCE: PCT Int. Appl., 552 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056015	A1	20050623	WO 2004-US41509	20041208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004162282	A1	20040819	US 2003-732897	20031209
PRIORITY APPLN. INFO.:			US 2003-732897	A 20031209
			US 2004-979882	A 20041101
			US 2002-453711P	P 20020612
			US 2003-460752	A2 20030611

OTHER SOURCE(S): MARPAT 143:78197
GI

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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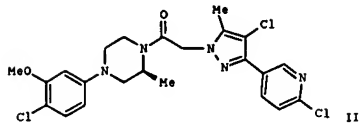
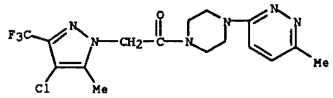
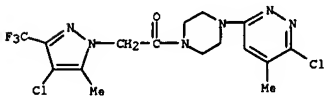


II

AB Title compds. I [wherein R1 = independently halo/cyclo/alkyl, alkenyl, alkynyl, amido, etc.; Ar1 = (un)substituted Ph, naphthyl, pyridyl, pyrazinyl, triazinyl, quinolinyl, etc.; HAr = (un)substituted heteroaryl selected from pyrazolyl, imidazolyl, triazolyl, tetrazolyl, etc.; L1 = (un)substituted linking group; m = 0-10; n = 1-2; with the proviso that certain compds. are absent; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as CCR1 receptor antagonists. For example, amination of 2-Chloro-1-[4-(4-chloro-3-methoxyphenyl)-2-(S)-methylpiperazin-1-yl]ethanone with 2-Chloro-5-(4-chloro-5-methyl-1H-pyrazol-3-yl)pyridine gave II. Selected I showed inhibition against CCR1 receptor with IC50 < 500 nM in chemotaxis and/or binding assays. Thus, I and their pharmaceutical compns. are useful for the treatment of CCR1-mediated diseases, and as controls in assays for the identification of competitive CCR1 antagonists.
IT 637020-32-7P 637020-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl piperazine derivs. as CCR1 receptor antagonists)
RN 637020-32-7 CAPLUS
CN Piperazine, 1-[[4-chloro-5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]acetyl]-4-(6-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



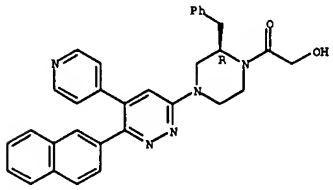
L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 637020-40-7 CAPLUS
CN Piperazine, 1-(6-chloro-5-methyl-3-pyridazinyl)-4-[[4-chloro-5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]acetyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:331950 CAPLUS
DOCUMENT NUMBER: 143:43843
TITLE: Design and synthesis of potent pyridazine inhibitors of p38 MAP kinase
AUTHOR(S): Tamayo, Nuria; Liao, Lillian; Goldberg, Martin; Powers, David; Tudor, Yan-Yan; Yu, Violeta; Wong, Lu Min; Henkle, Bradley; Middleton, Scot; Syed, Rashid; Harvey, Timothy; Jang, Graham; Hungate, Randall; Dominguez, Celia
CORPORATE SOURCE: Chemistry Research and Discovery, Amgen, Inc., Thousand Oaks, CA, 91320, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(9), 2409-2413
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Novel potent trisubstituted pyridazine inhibitors of p38 MAP (mitogen activated protein) kinase are described that have activity in both cell-based assays of cytokine release and animal models of rheumatoid arthritis. They demonstrated potent inhibition of LPS-induced TNF-α production in mice and exhibited good efficacy in the rat collagen induced arthritis model.
IT 853730-52-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and synthesis of potent pyridazine inhibitors of p38 MAP kinase)
RN 853730-52-6 CAPLUS
CN Piperazine, 1-(hydroxyacetyl)-4-[6-(2-naphthalenyl)-5-(4-pyridinyl)-3-pyridazinyl]-2-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



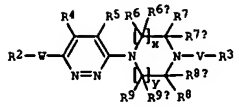
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120714 CAPLUS
DOCUMENT NUMBER: 142:219310
TITLE: Preparation of pyridazine derivatives as stearoyl-CoA desaturase inhibitors for the treatment of diabetes and other diseases
INVENTOR(S): Abrec, Melwyn; Chafeev, Mikhail; Chakka, Nagasree; Chowdhury, Sultan; Fu, Jian-Min; Gschwend, Heinz W.; Holladay, Mark W.; Hou, Duanjie; Kamboj, Rajender; Kodumuru, Vishnumurthy; Li, Wenbao; Liu, Shifeng; Raina, Vandna; Sun, Sengen; Sun, Shaoyi; Sviridov, Serguei; Tu, Chi; Winther, Michael D.; Zhang, Zaihui
PATENT ASSIGNEE(S): Xenon Pharmaceuticals Inc., Can.
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011655	A2	20050210	WO 2004-US24548	20040729
WO 2005011655	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005065143	A1	20050324	US 2004-901563	20040729
PRIORITY APPLN. INFO.:			US 2003-491095P P	20030730
			US 2004-546786P P	20040223
			US 2004-546815P P	20040223
			US 2004-546820P P	20040223
			US 2004-546898P P	20040223
			US 2004-546934P P	20040223
			US 2004-553403P P	20040316
			US 2004-553404P P	20040316
			US 2004-553416P P	20040316
			US 2004-553446P P	20040316
			US 2004-553491P P	20040316

OTHER SOURCE(S): MARPAT 142:219310
GI

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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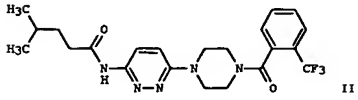


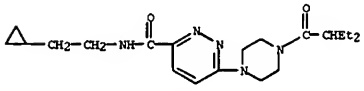
II

AB Title compds. I [wherein x, y = 1-3; W = C(O)N(R1), C(O)N[C(O)R1a], N(R1)C(O)N(R1) or N(R1)C(O); V = C(O/S) or C(R10)H; R1 = H or (un)substituted alkyl; R1a = H or (cyclo)alkyl; R2, R3 = alk(en)yl, (hetero)aryl or heterocyclyl; R4, R5 = H, F, Me, MeO or amine; R6, R6a, R7, R7a, R8, R8a, R9, R9a, R10 = H or alkyl; etc., and stereoisomers, enantiomers or tautomers, pharmaceutically acceptable salts, pharmaceutical compns. or prodrugs thereof] were prepared as stearoyl-CoA desaturase (SCD) inhibitors. For example, acylation of 1-Boc-piperazine with 2-trifluoromethylbenzoyl chloride followed by deprotection with TFA in dichloromethane gave the corresponding benzoylated piperazine. This compound underwent condensation with 3-amino-6-chloropyridazine, and the resultant 3-pyridazinamine was then coupled with 4-methylpentanoic acid to afford piperazinylpyridazine II. I and their pharmaceutical compns. are useful in the treatment of SCD-mediated diseases, such as diabetes, obesity and fatty liver.

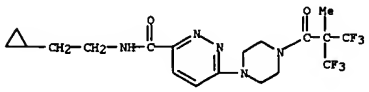
IT **840489-28-3P**, 6-[4-(2-Ethylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840489-38-5P**, 6-[4-(3,3,3-Trifluoro-2-methyl-2-trifluoromethylpropionyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840489-41-0P**, 6-[4-(2,2-Dimethylpropionyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-25-7P**, 6-[4-(2,2-Dimethylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-26-8P**, 6-[4-(2,2-Dimethylpentanoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-34-8P**, 6-[4-(4,4,4-Trifluorobut-2-enoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-36-0P**, 6-[4-(4,4,4-Trifluoro-3-hydroxy-3-trifluoromethylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-37-1P**, 6-[4-(4,4,4-Trifluoro-3-hydroxy-3-methylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-40-6P**, 6-[4-(4,4,4-Trifluoro-3-trifluoromethylbut-2-enoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide **840490-43-9P**, 6-[4-[2-(2-Trifluoromethylphenyl)acetyl]piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
840490-46-2P, 6-[4-(4,4,4-Trifluoro-3-methylbut-2-enoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide **840490-65-5P**, 6-[4-(4,4,4-Trifluoro-2-methylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide **840490-67-7P**, 6-[4-(4,4,4-Trifluoro-3-methylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide **840490-68-8P**, 6-[4-(4,4,4-Trifluorobutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide **840490-74-6P**, 6-[4-(3,3,3-Trifluoro-2-hydroxy-2-methylpropionyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; prepn. of piperazinylpyridazines as stearoyl-CoA desaturase inhibitors)

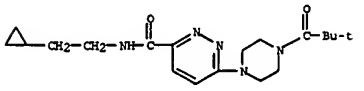
RN 840489-28-3 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-(2-ethyl-1-oxobutyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 840489-38-5 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-[3,3,3-trifluoro-2-methyl-1-oxo-2-(trifluoromethyl)propyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

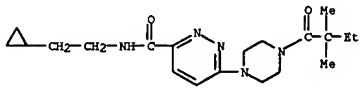


RN 840489-41-0 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-(2,2-dimethyl-1-oxopropyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 840490-25-7 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-(2,2-dimethyl-1-oxobutyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 840490-26-8 CAPLUS
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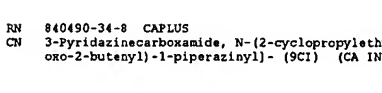
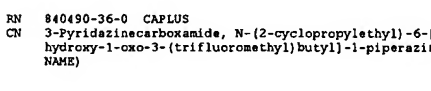
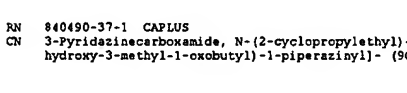


RN 840490-34-8 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-(4,4,4-trifluoro-1-oxo-2-butenyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

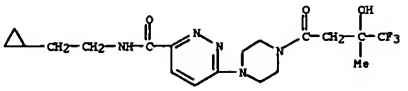


RN 840490-36-0 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-[4,4,4-trifluoro-3-hydroxy-1-oxo-3-(trifluoromethyl)butyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

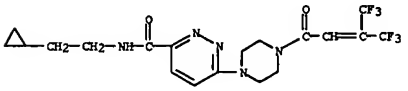


RN 840490-37-1 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-(4,4,4-trifluoro-3-hydroxy-3-methyl-1-oxobutyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 840490-40-6 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-[4,4,4-trifluoro-1-oxo-3-(trifluoromethyl)-2-butenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 840490-43-9 CAPLUS
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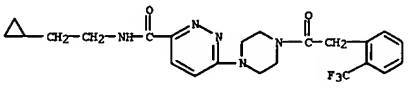

RN 840490-46-2 CAPLUS
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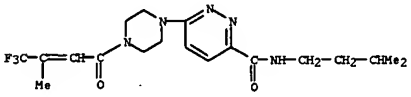
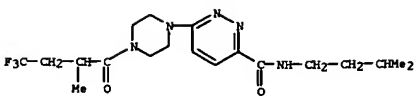
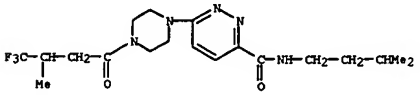


RN 840490-65-5 CAPLUS
CN 3-Pyridazinecarboxamide, N-(3-methylbutyl)-6-[4-(4,4,4-trifluoro-2-methyl-1-oxobutyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

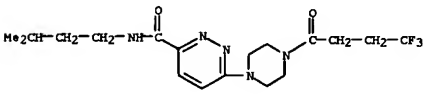
L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



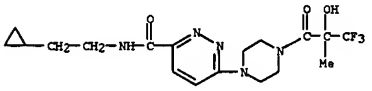
RN 840490-67-7 CAPLUS
CN 3-Pyridazinecarboxamide, N-(3-methylbutyl)-6-[4-(4,4,4-trifluoro-3-methyl-1-oxobutyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 840490-68-8 CAPLUS
CN 3-Pyridazinecarboxamide, N-(3-methylbutyl)-6-[4-(4,4,4-trifluoro-1-oxobutyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 840490-74-6 CAPLUS
CN 3-Pyridazinecarboxamide, N-(2-cyclopropylethyl)-6-[4-(3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:681396 CAPLUS
DOCUMENT NUMBER: 141:190799
TITLE: Preparation of substituted piperazines as CCR1 receptor antagonists
INVENTOR(S): Pennell, Andrew M. K.; Aggen, James B.; Wright, J. J. Kim; Sen, Subhabrata; McMaster, Brian E.; Dairaghi, Daniel Joseph
PATENT ASSIGNEE(S): Chemocentryx, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 178 pp., Cont.-in-part of U.S. Pat. Appl. 2004 82,571.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

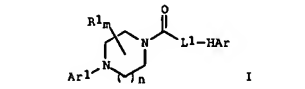
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004162282	A1	20040819	US 2003-732897	20031209
US 2004082571	A1	20040429	US 2003-460752	20030611
WO 2005056015	A1	20050623	WO 2004-US41509	20041208

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-453711P P 20020612
US 2003-460752 A2 20030611
US 2003-732897 A 20031209
US 2004-979882 A 20041101

OTHER SOURCE(S): MARPAT 141:190799
GI

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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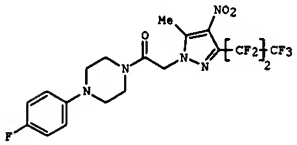
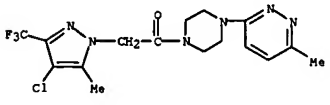


II

AB Title compds. presented by the formula I [wherein R1 = independently (halo)alkyl, cycloalkyl, alkenyl, alkynyl, amido, etc.; Ar1 = (un)substituted Ph, naphthyl, pyridyl, pyrazinyl, etc.; HAr = (un)substituted pyrazolyl, imidazolyl, triazolyl, etc.; L1 = (un)substituted linking; m = 0-10; n = 1-2; with provisos; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as CCR1 receptor antagonists. For example, reaction of 3-heptafluoropropyl-5-methyl-4-nitro-1H-pyrazole and 2-chloro-1-[4-(4-fluorophenyl)piperazin-1-yl]ethanone gave II. I showed inhibition against CCR1 receptor (e.g. IC50 = 0.112 μM for II). Thus, I and their pharmaceutical compns. are useful for the treatment of CCR1-mediated diseases, and as controls in assays for the identification of competitive CCR1 antagonists.

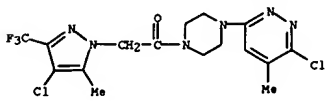
IT 637020-32-7P 637020-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl piperazines as CCR1 receptor antagonists)

RN 637020-32-7 CAPLUS
CN Piperazine, 1-[[4-chloro-5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]acetyl]-4-(6-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



RN 637020-40-7 CAPLUS
CN Piperazine, 1-(6-chloro-5-methyl-3-pyridazinyl)-4-[[4-chloro-5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]acetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



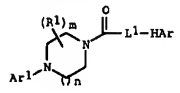
L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1006778 CAPLUS
DOCUMENT NUMBER: 140:42209
TITLE: Preparation of 1-aryl-4-substituted piperazine CCR1 antagonists for the treatment of inflammation and immune disorders
INVENTOR(S): Pennell, Andrew M. K.; Aggen, James B.; Wright, J. J. Kim; Sen, Subrabrata; McMaster, Brian E.; Dairaghi, Daniel Joseph
PATENT ASSIGNEE(S): Chemocentryx, Inc., USA
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

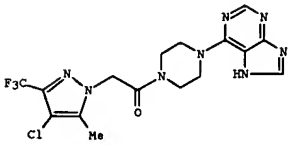
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105853	A1	20031224	WO 2003-US18660	20030611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2488202	AA	20031224	CA 2003-2488202	20030611
EP 1531822	A1	20050525	EP 2003-737057	20030611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-453711P P 20020612
WO 2003-US18660 W 20030611
OTHER SOURCE(S): MARPAT 140:42209
GI

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I

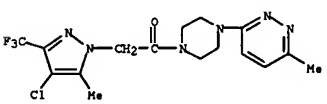


II

AB Title compds. I [n = 1-2; m = 0-10; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, etc.; Ar1 = Ph, naphthyl, pyridyl, etc.; HAr = pyrazolyl, imidazolyl, triazolyl, etc.; L1 = linking group having 1-3 chain atoms with some provisions] are prepared For instance, 2-[(4-chloro-5-methyl-3-trifluoromethylpyrazol-1-yl)-1-piperazinyl]ethanone (preparation given) is reacted with 6-chloropurine to give II. I are potent antagonists of the CCR1 receptor and are useful in the treatment of inflammation.

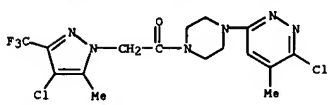
IT 637020-32-7P 637020-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-aryl-4-substituted piperazine CCR1 antagonists for treatment of inflammation and immune disorders)

RN 637020-32-7 CAPLUS
CN Piperazine, 1-[[4-chloro-5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]acetyl]-4-(6-methyl-3-pyridazinyl)- (9CI) (CA INDEX NAME)



RN 637020-40-7 CAPLUS
CN Piperazine, 1-(6-chloro-5-methyl-3-pyridazinyl)-4-[[4-chloro-5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]acetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



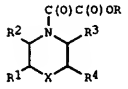
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:223755 CAPLUS
DOCUMENT NUMBER: 138:255254
TITLE: Preparation of oxamate derivatives with nitrogen part of six-membered heterocycle useful for treating hyperglycemia-related disorders
INVENTOR(S): Moinet, Gerard; Leriche, Gerard
PATENT ASSIGNEE(S): Lipha, Fr.
SOURCE: Fr. Demande, 43 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2829766	A1	20030321	FR 2001-11950	20010914
WO 2003024946	A2	20030327	WO 2002-EP9435	20020823
WO 2003024946	A3	20031204		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FR 2001-11950 A 20010914
OTHER SOURCE(S): MARPAT 138:255254
GI



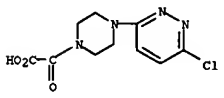
I

AB The invention relates to heterocyclic oxamates (shown as I; variables defined below; e.g. sodium (4-acetylpiperazino)oxoacetate), tautomeric, enantiomeric, diastereomeric and epimeric forms and pharmaceutically acceptable salts, methods for preparing them and use in treatment of pathologies associated with the hyperglycemia. For I: R = H, alkyl (C1-C3); X = O, S, -CR5R5'- or -NR6-; R1, R2, R3 and R4 = H or alkyl (C1-C3); addnl. details are given in the claims. The ability of 18 examples of I to reduce glycemia in diabetic rats is tabulated for 20 mg/kg/day after 1 and 4 days of treatment and also for 200 mg/kg/J after 1 and 4 days of treatment; for example, 18, 24, 16 and 18 %, resp., redns. were found for sodium (4-acetylpiperazino)oxoacetate. One example preparation of I is included, but characterization data is included for 155 examples of I.

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
For example, [4-(3-methoxyphenyl)piperazin-1-yl]oxoacetic acid was prepd. in 41% yield from reaction of 1-(3-methoxyphenyl)piperazine in THF with ethoxalyl chloride in toluene in the presence of K2CO3 followed by base hydrolysis of the formed ester. 2-Oxo-[4-(toluene-4-sulfonyl)piperazin-1-yl]acetic acid Et ester was prepd. in 54% yield by reacting piperazine with ethoxalyl chloride in acetic acid to give 2-oxo-2-piperazin-1-ylacetic acid Et ester hydrochloride followed by tosylation.

IT 502456-56-6P, (4-(6-Chloropyridazin-3-yl)piperazin-1-yl)oxoacetic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of oxamate derivs. with nitrogen part of six-membered heterocycle useful for treating hyperglycemia-related disorders)

RN 502456-56-6 CAPLUS
CN 1-Piperazineacetic acid, 4-(6-chloro-3-pyridazinyl)-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:76773 CAPLUS
DOCUMENT NUMBER: 138:137337
TITLE: Preparation of N-phenylsulfonyl-1,3-dihydro-2H-indol-2-one derivatives containing piperazinylcarbonyl or homopiperazinylcarbonyl as vasopressin receptor inhibitors, their preparation and their therapeutic use
INVENTOR(S): Di Malta, Alain; Garcia, Georges; Roux, Richard; Schoentjes, Bruno; Serradeil-le Gal, Claudine; Tonnerre, Bernard; Wagnon, Jean
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008407	A2	20030130	WO 2002-FR2500	20020715
WO 2003008407	A3	20031016		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

FR 2827604	A1	20030124	FR 2001-10359	20010717
FR 2827604	B1	20030919		
CA 2450437	AA	20030130	CA 2002-2450437	20020715
EP 1419150	A2	20040519	EP 2002-774822	20020715
EP 1419150	B1	20050427		

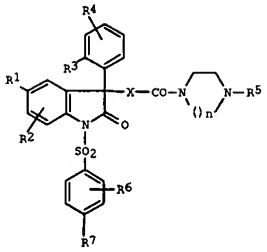
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002011284	A	20040803	BR 2002-11284	20020715
CN 1533387	A	20040929	CN 2002-814262	20020715
JP 2004536131	T2	20041202	JP 2003-513966	20020715
NZ 530144	A	20050324	NZ 2002-530144	20020715
AT 294171	E	20050515	AT 2002-774822	20020715
ZA 2003009717	A	20041215	ZA 2003-9717	20031215
US 2004180878	A1	20040916	US 2004-484370	20040116
HK 1061679	A1	20050722	HK 2004-104546	20040625

PRIORITY APPLN. INFO.: FR 2001-10359 A 20010717
WO 2002-FR2500 W 20020715

OTHER SOURCE(S): MARPAT 138:137337
GI

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



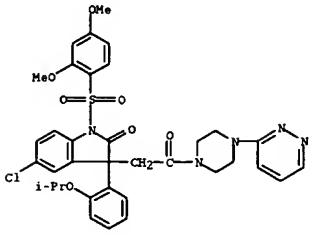
I

AB The invention concerns N-phenylsulfonyl-1,3-dihydro-2H-indole-2-one derivs. containing piperazinylcarbonyl or homopiperazinylcarbonyl (shown as I; variables defined below; e.g. 5-chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-3-(2-methoxyphenyl)-3-[2-oxo-2-[4-(4-pyridinyl)-1-piperazinyl]ethyl]-1,3-dihydro-2H-indol-2-one), as well as their addition salts with acids or organic salts, their solvates and/or hydrate(s), exhibiting affinity and selectivity for arginine-vasopressin V1b receptors and/or for oxytocin receptors, and further, for certain compds., an affinity for V1a receptors. The invention also concerns the method for preparing them, intermediate compds. (I without phenylsulfonyl) for their preparation, pharmaceutical compns. containing them and their use for preparing medicines. For I: n = 1 or 2; X = -CH2-, -O-, -NH-, -O-CH2-, -NH-CH2-, -NH-CH2-CH2-; R1 = halo, (C1-C4)alkyl, (C1-C4)alkoxy; R2 = H, halo, (C1-C4)alkyl, (C1-C4)alkoxy, trifluoromethyl; R3 = halo, (C1-C3)alkyl, (C1-C3)alkoxy, trifluoromethyl, trifluoromethoxy; R4 = H, halo, (C1-C3)alkyl, (C1-C3)alkoxy; R5 = pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazol-2-yl, oxazol-2-yl, imidazol-2-yl; R6 = (C1-C4)alkoxy; R7 = (C1-C4)alkoxy. Compds. I exhibit inhibition concns. (IC50) for V1a and V1b vasopressin receptors and for oxytocin receptors from 10-6 to 10-9 M and for V2 receptors better than 10-6 M. About 40 examples of intermediate prepns. and 92 examples of preparation of I are included.

IT 492432-09-4P, 5-Chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-3-(2-isopropoxyphenyl)-3-[2-oxo-2-[4-(pyridazin-3-yl)-1-piperazinyl]ethyl]-1,3-dihydro-2H-indol-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-phenylsulfonyldihydroindolone derivs. containing piperazinylcarbonyl or homopiperazinylcarbonyl as vasopressin receptor inhibitors, their preparation and their therapeutic use)

RN 492432-09-4 CAPLUS
CN Piperazine, 1-[[5-chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-2,3-dihydro-3-[2-(1-methylethoxy)phenyl]-2-oxo-1H-indol-3-yl]acetyl]-4-(3-pyridazinyl)- (9CI) (CA INDEX NAME)

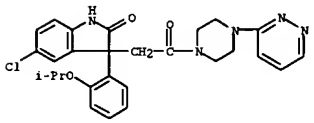
L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT **492431-87-5P**, 5-Chloro-3-(2-isopropoxyphenyl)-3-[2-oxo-2-[4-(pyridazin-3-yl)-1-piperazinyl]ethyl]-1,3-dihydro-2H-indol-2-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-phenylsulfonyldihydroindolone derivs. containing piperazinylcarbonyl or homopiperazinylcarbonyl as vasopressin receptor inhibitors, their preparation and their therapeutic use)

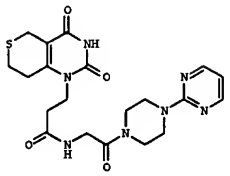
RN 492431-87-5 CAPLUS

CN Piperazine, 1-[[5-chloro-2,3-dihydro-3-[2-(1-methylethoxy)phenyl]-2-oxo-1H-indol-3-yl]acetyl]-4-(3-pyridazinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:767295 CAPLUS
DOCUMENT NUMBER: 138:137076
TITLE: Substituted uracil derivatives as potent inhibitors of poly(ADP-ribose)polymerase-1 (PARP-1)
AUTHOR(S): Steinhagen, Henning; Gerisch, Michael; Mittendorf, Joachim; Schlemmer, Karl-Heinz; Albrecht, Barbara
CORPORATE SOURCE: Institute of Medicinal Chemistry, Pharma Research Centre, Bayer AG, Wuppertal, D-42096, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3187-3190
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:137076
GI



I

AB A new class of PARP-1 inhibitors, namely substituted fused uracil derivs. such as I, were synthesized. Starting from a derivative with an IC50=2 μM the chemical optimization program led to compds. with more than a 100-fold increase in potency (IC50<20 nM). Addnl., physicochem. and pharmacokinetic properties were evaluated. It could be shown that compds. bearing a piperazine or Ph substituted βAla-Gly side chain exhibited the best overall profile.

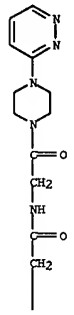
IT **491837-62-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of uracil derivs. as inhibitors of poly(ADP-ribose)polymerase-1)

RN 491837-62-8 CAPLUS

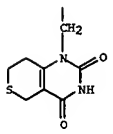
CN 2H-Thiopyrano[4,3-d]pyrimidine-1(5H)-propanamide, 3,4,7,8-tetrahydro-2,4-dioxo-N-[2-oxo-2-[4-(3-pyridazinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



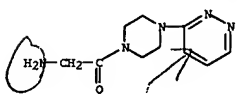
PAGE 2-A



IT **491837-79-7P 491837-85-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of uracil derivs. as inhibitors of poly(ADP-ribose)polymerase-1)

RN 491837-79-7 CAPLUS

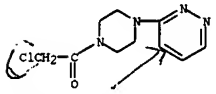
CN Piperazine, 1-(aminoacetyl)-4-(3-pyridazinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

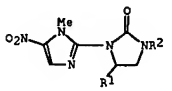
RN 491837-85-5 CAPLUS

CN Piperazine, 1-(chloroacetyl)-4-(3-pyridazinyl)- (9CI) (CA INDEX NAME)

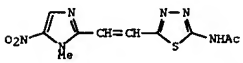


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

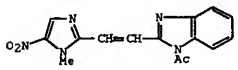
L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:528058 CAPLUS
DOCUMENT NUMBER: 117:128058
TITLE: Nitroimidazoles, part XXIII - activity of satranidazole series against anaerobic infections
AUTHOR(S): Nagarajan, K.; Gowrishankar, R.; Arya, V. P.; George, T.; Nair, M. D.; Shenoy, S. J.; Sudarsanam, V.
CORPORATE SOURCE: Hind. CIBA-GEIGY Res. Cent., Bombay, 400 063, India
SOURCE: Indian Journal of Experimental Biology (1992), 30(3), 193-200
CODEN: IJEBA6; ISSN: 0019-5189
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



III



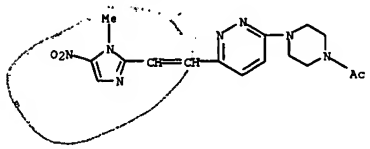
VI



VII

AB A large number of nitroimidazoles were examined for in vitro activity against 3 anaerobes - Bacteroides fragilis (Bf), a strain of Bf resistant to metronidazole (I) and Clostridium perfringens and many found to be active. Among these may be mentioned 1-methyl-5-nitroimidazoles carrying N-bound heterocycles at position 2, such as satranidazole (II) and III (R1 = H, R2 = SO2Et, SO2NMe2, morpholinylcarbonyl, morpholinoethylaminothioxomethyl) which are at least twice as active as I, ornidazole (IV) and tinidazole (V). Even more active are 5-nitroimidazolylbenzimidazole, -thiazolidinone, and -thiadiazolidine dioxide. Many other types of compds. derived from 1-methyl-2-amino-5-nitroimidazole are feebly active. Among 5-nitroimidazoles with a carbon substituent at position 2, I, IV and V are equiactive while dimetridazole is more active than I against Bf. Some 2-vinyl derivs. are very potent, with VI and VII being outstanding. Activity better than I is seen for nitroimidazooxazepines. 5-Nitroimidazoles are more active against anaerobes than the 4-nitro isomers. Antianaerobic and antiamoebic activities generally run parallel in these classes of compds. The study has led to the elaboration of the

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
antianaerobic profile of II.
IT 87008-25-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anaerobic bacteria sensitivity to, structure in relation to)
RN 87008-25-1 CAPLUS
CN Piperazine, 1-acetyl-4-[6-[2-(1-methyl-5-nitro-1H-imidazol-2-yl)ethenyl]-3-pyridazinyl]- (9CI) (CA INDEX NAME)

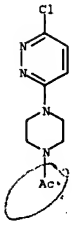


L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:129918 CAPLUS
DOCUMENT NUMBER: 104:129918
TITLE: Anti-virally active pyridazinamines
INVENTOR(S): Stokbroekx, Raymond Antoine; Van der Aa, Marcel Jozef Maria; Willems, Joannes Josephus Maria; Luyckx, Marcel Gerebernus Maria
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: Eur. Pat. Appl., 76 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

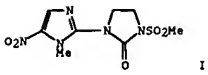
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 156433	A2	19851002	EP 1985-200384	19850315
EP 156433	A3	19860723		
EP 156433	B1	19910227		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 5001125	A	19910319	US 1985-702772	19850215
AT 61050	E	19910315	AT 1985-200384	19850315
CZ 277730	B6	19930317	CZ 1985-1952	19850320
NO 8501167	A	19850927	NO 1985-1167	19850322
NO 161257	B	19890417		
NO 161257	C	19890726		
ES 541521	A1	19860416	ES 1985-541521	19850322
SU 1384198	A3	19880323	SU 1985-3867689	19850322
DK 8501341	A	19850927	DK 1985-1341	19850325
DK 166277	B	19930329		
DK 166277	C	19930830		
FI 8501177	A	19850927	FI 1985-1177	19850325
FI 85373	B	19911231		
FI 85373	C	19920410		
AU 8540348	A1	19851003	AU 1985-40348	19850325
AU 576563	B2	19880901		
JP 60226862	A2	19851112	JP 1985-58636	19850325
HU 37614	A2	19860123	HU 1985-1127	19850325
HU 198010	B	19890728		
ZA 8502235	A	19861126	ZA 1985-2235	19850325
IL 74707	A1	19880531	IL 1985-74707	19850325
CA 1238321	A1	19880621	CA 1985-477330	19850325
PL 147465	B1	19890630	PL 1985-252562	19850325
RO 91197	B3	19870630	RO 1985-118137	19850326
US 5157035	A	19921020	US 1991-637091	19910103
US 5292738	A	19940308	US 1992-929622	19920813
PRIORITY APPLN. INFO.:			US 1984-593444 A	19840326
			US 1985-702772 A	19850215
			EP 1985-200384 A	19850315
			US 1991-637091 A3	19910103

GI For diagram(s), see printed CA Issue.
AB The title compds. I [R1 = H, halo, 1H-imidazol-1-yl, alkyloxy, aryloxy, aralkoxy, alkylthio, arylthio, HO, HS, amino, alkylsulfinyl, alkylsulfonyl, cyano, alkoxycarbonyl, alkanoyl, alkyl; R2, R3 = H, alkyl; R2R3 = CH:CHCH:CH; X = CH:NCH:CH2, optionally alkyl- or aryl-substituted CmH2mNR4CnH2n, CmH2mCR5R6CnH2n, Cm-1H2(m-1)CR7:CR8CnH2n; R4 = H, alkyl, aryl, thiazolyl, pyrimidinyl, quinolinyl, etc.; R5 = H, alkyl, aryl, HO, alkyloxy, etc.; R6 = H, alkyl, aryl, indolyl, pyridinyl, etc.; R7, R8 = H, alkyl, aryl, aralkyl, pyridinyl; aryl = (un)substituted Ph; m,n = 1-4; m+n = 3-5] were prepd. Thus, 3,6-dichloropyridazine was treated with 1,2,3,6-tetrahydro-4-(3-methylphenyl)pyridine to give pyridinylpyridazine II, which in the Rhinovirus Cytopathic Effect Test gave 0.006 μg/mL as the lowest concn. necessary to inhibit ≥75% of the cytopathic effect of human rhinovirus. Oral drops were prepd. by dissolving 500 g I in 0.5 L MeCHOHCO2H and 1.5 L polypropylene glycol at 60-80°, cooling to 30-40°, adding 35 L polyethylene glycol, mixing well, adding 1750 g Na saccharin in 2.5 L purified H2O and 2.5 L cocoa flavor, and finally polyethylene glycol to 50 L to provide a soln. comprising 10 mg I/mL.

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
IT 100241-18-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as virucide)
RN 100241-18-7 CAPLUS
CN Piperazine, 1-acetyl-4-(6-chloro-3-pyridazinyl)- (9CI) (CA INDEX NAME)

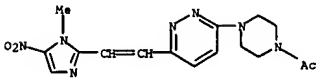


L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:603875 CAPLUS
DOCUMENT NUMBER: 101:203875
TITLE: Nitroimidazoles: part XIX - structure-activity relationships
AUTHOR(S): Nagarajan, K.; Arya, V. P.; George, T.; Nair, M. D.; Sudarsanam, V.; Ray, D. K.; Shrivastava, V. B.
CORPORATE SOURCE: Res. Cent., CIBA-GEIGY, Bombay, 400 063, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1984), 23B(4), 342-62
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

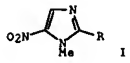


I

AB A variety of nitroimidazoles, mostly 1,2-disubstituted-5-nitro derivs. were examined for in vitro activity against Entamoeba histolytica and for effectiveness in treating early hepatic infection in golden hamsters. Many compds. carried a functionalized N atom at position 2. In vivo activity was observed with 1-alkyl-5-nitroimidazoles carrying a substituted imidazolidinone or imidazole. Among these derivs., 1-methylsulfonyl-3-(1-methyl-5-nitro-2-imidazolyl)-2-imidazolidinone (I) [56302-13-7] was the most potent against hepatic and caecal infections of E. histolytica in the golden hamster and Trichomonas foetus infections in mice. It was developed as a drug for treatment of amoebiasis, giardiasis, and trichomoniasis. The structure-antiamebic activity relationships of the nitroimidazoles are discussed.
IT 87008-25-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amebicidal activity of, structure in relation to)
RN 87008-25-1 CAPLUS
CN Piperazine, 1-acetyl-4-[6-[2-(1-methyl-5-nitro-1H-imidazol-2-yl)ethenyl]-3-pyridazinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:522370 CAPLUS
DOCUMENT NUMBER: 99:122370
TITLE: Nitroimidazoles: Part XV. 1-Methyl-5-nitro-2-oxy(mercapto)imidazoles, 1-methyl-5-nitroimidazole-2-methanol (carboxaldehyde and glyoxalic ester) derivatives and 1-substituted alkyl-2-methyl-5- and -4-nitroimidazoles
AUTHOR(S): Arya, V. P.; Nagarajan, K.; Shenoy, S. J.
CORPORATE SOURCE: Ciba-Geigy Res. Cent., Bombay, 400 063, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1982), 21B(12), 1078-86
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Approx. 60 title imidazoles were prepared by standard reactions. Thus, displacement reactions on I (R = MeSO2) with phenols gave I (R = p-OCHC6H4, 1-oxido-3-pyridyl).
IT 87008-25-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 87008-25-1 CAPLUS
CN Piperazine, 1-acetyl-4-[6-[2-(1-methyl-5-nitro-1H-imidazol-2-yl)ethenyl]-3-pyridazinyl]- (9CI) (CA INDEX NAME)